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Research Article

Factors affecting long-term remission in patients with FSGS and NS.

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Abstract

In FSGS with Nephrotic Syndrome (NS) 23 patients (61%) of 38 with functional outcome are in remission with very long follow up (from 60 to 331 months) after treatment with Steroids alone or in combination with Cyclophosphamide.

It would be interesting to assess whether in 11 patients with follow up from 5 to 27.6 years some parameters are associated with less severe disease favouring very long term remission.

Three parameters were considered [age<vs≥35 yrs, normal or high blood pressure (BP0 and BP1) baseline 24hP <vs≥ 6.5] to verify whether they assess lower disease severity favouring remission.

Age≥ vs <35 yrs and BP1 va BP0 are characterized by very significant differences of age, baseline and last eGFR, TID score and AH score. The patients with baseline 24hP < vs ≥6.5) were significantly different only for proteinuric parameters (TUP/C, IgG/C, Alb/C, α1m/C).

In all remission patients the last value of 24hP is not significantly different according to the considered parameters and is independent from the baseline values eGFR and TUP/C and duration of follow up.

Keywords: high blood pressure ; Nephrotic Syndrome; Cyclophosphamide

Introduction

In the last years several studies evaluated which is the most favourable prognostic factor for long-term stable renal function and remission of proteinuria in Focal Segmental Glomerulosclerosis (FSGS) with nephrotic syndrome (NS) (1-15). In observational studies proteinuric biomarkers based on high molecular weight proteins excretion such as IgG and α2-macroglobulin showed a high predictive value for remission in patients treated with steroids and Cyclophosphamide. The functional outcomes in all patients treated with Steroids alone or in combination with Cyclophosphamide include remission, persistent NS (PNS) with normal renal function (NRF) or chronic renal failure (CRF), and progression to ESRD. The interesting aim of this study is to assess if the very long follow up of patients with remission (159±77, 60-331) may be dependent on clinical, functional, histologic and proteinuric markers associated with less severe disease favouring a very long follow up of remission.

Patients and methods

The patients cohort included in the study was not selected. The patients attending the Nephrology and Dialysis Unit of San Carlo Borromeo Hospital, Milan, Italy, between January 1992 and April 2006 with renal biopsy diagnosis of Focal Segmental Glomerulosclerosis (FSGS) were 46; at baseline 6 patients have persistent non-nephrotic proteinuria (<3.5 g/24h), 40 patients have nephrotic syndrome (proteinuria ≥3.5 g/24h and/or serum albumin <3.0 g/dL). The inclusion criteria were: at least six glomeruli in renal biopsy; typical features at light and immunofluorescence microscopy. The functional outcomes was available for 38 NS patients with rather long follow up: mean 111±87 months (12-331). Three types of outcome were considered: 1) Remission of NS: complete: proteinuria ≤ 0.30 g/24hP; partial: proteinuria ≤ 2.0 g/24hP; 2) persistent NS (PNS) with long lasting normal renal function (NRF) or chronic renal failure (CRF); 3) progression to end-stage renal disease (ESRD). Among patients with NS and outcome (n. 38) 23 (61%) developed remission, 2 patients (5%) have persistent NS (PNS) with normal renal function (NRF), 4 patients (11%) have PNS with (CRF) and 9 patients (24%) progressed to end stage renal disease (ESRD). The follow up of patients with remission is rather long [(from 60 to 331 months) (5 to 27.6 years)]. The treatment of all the 38 patients with functional outcome were: Steroids alone or Steroids in combination with cyclophosphamide: in Remission: Steroids alone (n. 5); Steroids and Cyclo (n. 18); in PNS with NRF: Steroids alone (n. 1); Steroids and Cyclo

(n. 1); in PNS with CRF: Steroids alone (n. 3), Steroids and Cyclo (n. 1); ESRD: Steroids alone n. 1; Steroids and Cyclo n. 8 (89%). The objective of the study is to evaluate whether some factors are associated with the outcome remission with very long follow up. Several parameters were considered: age < vs ≥ 35 years, blood pressure [normal or high (BP0 < 140/90, BP1 ≥ 140/90), baseline 24 hours proteinuria (24hP <vs≥6.5), follow up <or ≥180 months. The treatment was with Steroids alone or steroids in combination with cyclophosphamide. The end point considered was the last value of 24 hours proteinuria. Three types of outcome were considered: 1) Remission of NS: complete: proteinuria ≤ 0.30 g/24h; partial: proteinuria ≤ 2.0 g/24h; 2) persistent NS with long lasting normal renal function (NRF) or chronic renal failure (CRF); 3) progression to end-stage renal disease (ESRD) (Table 1).

Laboratory analysis

Proteinuria was measured in 24 hour urine collection and second morning urine sample by the Coomassie blue method (modified with sodium-dodecyl-sulphate) and expressed as 24/hour proteinuria and protein creatinine/ratio (mg urinary protein/g urinary creatinine). Serum and urinary creatinine were measured enzymatically and expressed in mg/dL. Serum albumin and IgG and urinary IgG, α2-macroglobulin (α2m), Albumin and α1-microglobulin (α1m) were measured by immunonephelometry; urinary proteins were expressed as urinary protein/creatinine ratio (IgG/C, α2m/C, Alb/C, α1m/C). Estimated glomerular filtration rate (eGFR) was measured by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula (16). Three types of renal lesion that are markers of disease severity in any type of GN were evaluated: percentage of glomeruli with global glomerulosclerosis (GGS%); extent of tubulo-interstitial damage (TID) evaluated semi-quantitatively by a score: tubular atrophy, interstitial fibrosis and inflammatory cell infiltration graded 0, 1 or 2 if absent, focal or diffuse (TID global score: 0-6) and extent of Arteriolar Hyalinosis (AH) evaluated semiquantitatively by a score: 0, 1, 2, 3 if absent, focal, diffuse, diffuse with lumen reduction, respectively (AH global score 0-4).

Statistical analysis

Continuous variables are expressed as means±SD. Categorical variables are expressed as the number of patients (%). The differences of mean were determined by t-test; categorical variables by the chi-square test. All statistical analyses were performed using Stata 15.1 (StataCorp LP, TX, USA). Two-sided p<0.05 was considered statistically significant.

Results

In 38 patients with NS and functional outcome 23 patients (61%) developed remission: the remission patients with age <35 years were 12 and those with age ≥ 35 years were 11. They were significantly different for age (p = 0.001), baseline eGFR (p <0.0001), last eGFR (p = 0.04), TID score (p = 0.005), AH score (p = 0.01); the baseline 24h P was 7,3 and 7.1, respectively; the last 24hP was 0.37 and 0.30, respectively (p = 0.77) (Table 1) The patients with BP0 were 10 and those with BP1 were 13; they were significantly different for age (p = 001), baseline eGFR (p <0.0001), last eGFR (p =0.04), TID score (p =0.001) and AH score (p=0.017); baseline 24hP was 6.3 and 7.9, respectively (p =0.18); last 24hP was 0.29 and 0.37 respectively (p = 0.71). The patients with follow up < 180 months were 11 and those with follow up ≥ 180 months were 12; no one of the clinical, functional, histologic and proteinuric parameters was significantly different between them; baseline 24hP was 8.0 and 6.0, respectively (p = 0.29); the last 24hP was 0.36 and 0.32, respectively (p=0.85); the follow up was significantly different (91 vs 221 months, p <0.0001). The patients with baseline 24hP < 6.5 were 13 and those with baseline 24hP ≥ 6.5 were 10. The patients with 24hP < 6.5 and those with 24hP ≥ 6.5 were significantly different for TUP/C (p=0.0001), IgG/C (p=0.04), Alb/C (p=0.0002) and α1m/C (p=0.006) and 24hP (p=0.001); the last 24hP was 0.36 and 0.30, respectively (p = 0.74). In conclusion the factors affecting remission were age, blood pressure and baseline 24hP. but the last 24hP was not significantly different between the considered parameters or according the baseline values of eGFR and TUP/C. Thus no one of the considered factors is associated with significantly different values of last 24hP and duration of remission (Table 2).

Discussion

In the 23 patients with remission the follow up is rather long (from 60 to 331 months); it would be interesting to assess whether the patients with very long follow (27.6 years) were characterized by clinical, functional, histologic and proteinuric markers less severe than in patients with lower follow up. The last value of 24hP is not significantly different according to the baseline markers of severity of disease (age, normal or high blood pressure, baseline 24hP) (Table 3). Thus no one factor has been identified as associated with the duration of follow up. Few patients after remission show recurrence of NS that was still responsive to the first treatment. It may be suggested that the patients characterized by markers associated with more severe disease (age, blood pressure, baseline 24hP) should be treated with higher dosage and longer duration of the treatment that developed the first remission.

FSGS & NS n. 38	Age	Basel. eGFR	Last eGFR	Follow up (mts)	TUP/C	IgG/C	Alb/C	α1m/C	GGS%	TID sc	AH sc	Last 24h/P	High BP %
Remission n. 23	41.5±17.3	86.3±30.9	84.3±32	159±76	5223± 3469	165±158	4599±3170	35.2± 23.5	5.4±7.1	1.59±1.33	0.22±043	0.34±0.53	n. 13 (57%)
PNS & NRF n. 2	38.5±16.2	77.5±45.9	89.0±26.8	61±18	3072± 715	68±44	1100± 245	15.0± 7.2	22.5±0	3.5±1.4	2.00±7.2	7.01±1.39	n. 1 (50%)
PNS & CRF n. 4	38.0±17	55.7±11.4	45.5±14.6	30±4	3464± 1698	205±175	2647± 707	27.9±11	20.0± 14.8	3.0±1.0	0.66±11	3.61±3,62	n. 2 (50%)
ESRD n. 9	33.3±21.3	76.4±30.1	7.0±0	34±35	10477± 4098	353±123	8114± 3087	76.7±28.6	7.4±13.0	2.00±2.07	0.75±28.6	12.5±8.7	n. 5(56%)
P Rem vs ESRD	0.32	0.42	<0.0001		0.005	0.015	0.011	0.002	0.69	<0.0001	0.15	0.003	.

Table 1. *Clinical, functional, histologic and proteinuric parameters in patients with Focal Segmental Glomerulosclerosis (FSGS) with different outcome.*

NS Remission n. 23	*Age*	*Bas.eGFR*	*Last eGFR*	*Follow up*	*TUP/C*	*IgG/C*	*Alb/C*	*a1m/C*	*GGS%*	*TID sc*	*AH sc*	*Last 24hP*	*Basel. 24hP*
Basel. 24hP < 6.50 n. 13	44.2±8.9	90.2±29.5	79.5±2.4	179±44	2963± 3169	109±33	2690± 4210	23.5± 11.4	6.6±6.9	1.61±1.31	0.23±0.37	0.36±0.47	5.3
Basel. 24hP ≥ 6.50 n. 10	37.9±3.0	81.3±34.4	90.5±41	133±45	8163± 3976	238±157	7211± 4609	50.5± 20.9	3.7±7.8	1.55±1.32	0.22±050	0.30±0.60	9.8
	0.38	0.50	0.46	0.14	0.0001	0.048	0.0002	0.006	0.32	0.92	0.96	0.76	0.001
Normal press, BP0 n. 10	29.6±5.4	111.3±32.1	98.±27	149±24	4382± 3287	114±26	4075± 2747	25.9± 9.9	2.9±4.6	0.50±1.33	0.23±0.42	0.29±0.05	6.3
High press. BP1 n. 13	50.6±17.8	71.6±32.1	73.5±36	167±47	5871± 3716	204±160	5002± 2246	42.4±21	7.5±8.7	2.50±1.16	0.42±0.45	0.37±0.66	8.0
	<0.0001	0.0004	0.0007	0.35	0.98	0.32	0.89	0.32	0.66	0.003	0.016	0.39	0.55
Age < 35 years n. 11	27.2±3.6	110.1±29.6	108±26	146±31	5168± 3286	126±29	4552± 3166	30.6± 11.6	4.7±7.2	0.82±1.40	0.23±0.40	0.23±0-08	7.5
Age ≥ 35 years n. 12	54.6±19.3	64.6±33.4	62.6±37.4	171±45	5275± 3776	201	4642± 2326	39.4± 21.7	6.1±7.4	2.36±1.18	0.45±0.46	0.43±0.68	7.0
	<0.0001	<0.0001	0.0002	0.44	0.94	0.26	0.95	0.02	0.66	0.003	0.016	0.40	0.71
Follow up <180 mts n. 11	41±19	85.4±26.9	83.7±26.5	91±31	5239± 3286	222±29	4777± 3166	32.6± 11.6	3.7±7.2	1.27±1.40	0.23±0.18	0.36±0-08	5.1
Follow up ≥180 mts n. 12	42±17	87.2±33.4	84.7±37.4	221±45	5210± 3776	113±160	4436± 2326	37.6±22	7.1±7.4	1.90±1.18	0.27±0.27	0.31± 0.68	9.2
	0.88	0.89	0.12	<0.0001	0.98	0.11	0.80	0.62	0.28	0.27	0.63	0.85	0.29

Table 2. *Clinical, functional, histologic and proteimuric parameters in remission patients according to basel. 24hP, normal or high blood pressure (BP0 and BP1), age<vs≥35 years, follow up<vs≥180 months.*

FSGS & NS Remission n. 23 n. 38	Last 24hP	Last 24hP
FSGS Remission all 23 patients	0.34	
Age < vs ≥ 35 years	0.37	0.30
BP 0 vs BP 1	0.29	0.37
Baseline 24hP < vs ≥ 6.5	0.36	0.30
Follow up < vs ≥ 180 months	0.36	0.32

Table 3. *Last value of 24hP in all 23 remission patients, in patients with age <vs≥35 yrs, BP0 vs BP1, baseline 24hP <vs≥ 6.50, follow up < vs ≥ 180 months.*

References

1. C. Bazzi. (2016) Prediction of ESRD and long-term remission by proteinuric markers in primary focal segmental glomerulosclerosis with nephrotic syndrome: a review. Nephrology and Renal Disease. Vol 1, pp 38-43.
2. C. Bazzi, V. Rizza, D. Casellato, G. Stivali, G. Rachele, P. Napodano, M. Gallieni and G. D'Amico. (2013) Urinary IgG and α2-Macroglobulin Are Powerful Predictors of Outcome and Responsiveness to Steroids and Cyclophosphamide in Idiopathic Focal Segmental Glomerulosclerosis with Nephrotic Syndrome. BioMed Research International. Vol 2013, Article ID 941831, pp1-8.
3. C. Bazzi. Prediction of ESRD and long-term remission by proteinuric markers in primary focal segmental glomerulosclerosis with nephrotic syndrome: a review. Nephrology and Renal Disease. Vol 1(2) pag. 38-43; doi: 10.15761/NRD. 1000108.
4. M. M. Lowik, P. J. Groenen, E. N. Levtchenko, L. A. Monnens, and L. P. (2009) van den Heuvel, "Molecular genetic analysis of podocyte genes in focal segmental glomerulosclerosis—a review," European Journal of Pediatrics, vol. 168, no. 11, pp. 1291–1304.
5. R. Gbadegesin, P. Lavin, J. Foreman, and M. Winn, (2011) "Pathogenesis and therapy of focal segmental glomerulosclerosis: an update," Pediatric Nephrology, vol. 26, no. 7, pp. 1001–1015.
6. I. M. Rood, J. K. Deegens, and J. F. Wetzels, (2012) "Genetic causes of focal segmental glomerulosclerosis: implications for clinical practice", Nephrology Dialysis Transplantation, vol. 27, no. 3, pp.882–890.
7. M. J. Chun, S. M. Korbet, M.M. Schwartz, and E. J. Lewis, (2004) "Focal segmental glomerulosclerosis in nphrotic adults: presentation, prognosis, and response to therapy of the histologic variants," Journal of the American Society of Nephrology, vol. 15, no. 8, pp. 2169–2177.
8. A. Meyrier, (2009) "An update on the treatment options for focal segmental glomerulosclerosis," Expert Opinion on Pharmacotherapy, vol. 10, no. 4, pp. 615–628.
9. J. K. J. Deegens, E. J. Steenbergen, and J. F.M.Wetzels, (2008) "Review on diagnosis and treatment of focal segmental glomerulosclerosis,"Netherlands Journal of Medicine, vol. 66, no. 1, pp. 3–12.
10. A. Y.Meyrier, (2009) "Treatment of focal segmental glomerulosclerosis with immunophillin modulation: when did we stop thinking about pathogenesis?" Kidney International, vol. 76, no. 5, pp.487–491.
11. A. Meyrier, "Treatment of glomerular disease with cyclosporine A," Nephrology Dialysis Transplantation, vol. 4, no. 11, pp. 923–931, 198
12. A.Meyrier, (2003) "Treatment of idiopathic nephrosis by immunophillin modulation," Nephrology Dialysis Transplantation, vol. 18, no. 6, pp. vi79–vi86.
13. J. Hardwicke, R. H. R. White, and A. Williams, , (1976) "Molecular size of IgG in patients with focal glomerulosclerosis," Clinical Nephrology, vol. 6, no. 1, pp. 290–294.
14. C. Bazzi, C. Petrini, V. Rizza et al., , (2003) "Fractional excretion of IgG predicts renal outcome and response to therapy in primary focal segmental glomerulosclerosis: a pilot study,"TheAmerican Journal of Kidney Diseases, vol. 41, no. 2, pp. 328–335, 2003.
15. V. D. D'Agati, A. B. Fogo, J. A. Bruijn, and J. C. , (2004) Jennette. Pathologic classification of focal segmental glomerulosclerosis:a working proposal," The American Journal of Kidney Diseases, vol. 43, no. 2, pp. 368–382.
16. A. S. Levey, L. A. Stevens, C. H. Schmid et al., , (2009) "A new equation to estimate glomerular filtration rate," Annals of Internal Medicine, vol. 150, no. 9, pp. 604–612.

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